REMARKS

The above amendments essentially are those suggested by the Examiner, except that the subject matter of the suggested claims were combined into independent claim 1. Accordingly, no new matter issue arises, and entry of the amendments is requested respectfully.

I. In item 4, claims 1-3, 7, 8, 27, 28, 30, 31 and 43-47 were rejected under 35 U.S.C. 102(b) over WO99/26480). The Examiner relies in part on claim 33 of the WO document.

The rejection is traversed for the following reasons.

There is precedent that stands for the proposition that a mere "shotgun" recitation of a number of species of a genus, does not always anticipate every species contained therein.

When a reference does not highlight a specific element from a genus of possible elements, anticipation does not exist as to that specific element. In re Kollman et al. (CCPA 1979) 595 F2d 48, 201 USPQ 193. Moreover, when the various species of a genus are typified by divergent properties, anticipation does not lie. In re Kalm (CCPA 1967) 378 F2d 959, 154 USPQ 10. A generic formula of a vast number of species

does not anticipate all species encompassed therein merely because they fall within the scope of the formula. In re Ruschig et al. (CCPA 1965) 343 F2d 965, 145 USPQ 274.

WO99/26480 ("the PCT") teaches at pages 11-14 possibly all conceivable means for administering a biological drug. An artisan would have a large list of delivery means from which to choose and to test to obtain the instantly claimed invention, and it is well known that different delivery means can have an impact on bioavailability. There is no highlighting and teaching of direct administration to the eye as claimed in the instant application.

The working examples teach only ex vivo transduction and engraftment of the transformed cells by standard subcutaneous, intravenous or intraperitoneal implantation. None of the working examples teaches direct administration of a vector to the eye. As noted in the paragraph bridging pages 13 and 14 of the PCT, transfer of the nucleic acid is the critical first step in gene therapy.

The PCT also is focused primarily on treating cancer, see for example, the sentence bridging pages 7 and 8, and the working examples.

Angiogenesis is a complicated process. Numerous different effector cells are involved and angiogenesis varies from tissue to tissue, and varies between normal tissues and diseased tissues. For example, Eberhard et al., Cancer Research 60, 1388-1393, 2000, teach that angiogenesis is heterogeneous, and little is known about how the process occurs in human tumors, page 1388, right column, first full paragraph.

Carmeliet, Nature Medicine 9, 653-660, echoes the conclusion that angiogenesis is a complex interplay or multiple molecular signals, paragraph bridging pages 658 and 659.

Moreover, angiogenesis varies from tissue to tissue and between cancer and non-cancer occurrences. Campochiaro & Hackett, Oncogene 22, 6537-6548, 2003, teaches that a large number of proteins participate in complex ways. Each environment is unique and angiogenesis varies, first two sentences of the Abstract and the paragraph bridging the columns on page 6537. Benezra & Rafii, Cancer Cell, 205-206, March 2004, also teach that vascular beds vary from tissue to tissue and in cancer, see page 206, middle column, first full paragraph.

Thus, angiogenesis is a complex phenomenon that relies on different inducers and involves different molecules, cells and environments. Thus, angiogenesis in cancer is likely different from angiogenesis is a normal tissue. Also, angiogenesis in the placenta is likely different from angiogenesis in the newborn eye. Clearly, then, treatment of angiogenesis in a cancer does not predict successful treatment of angiogenesis in a normal tissue, and particularly in a specific tissue.

Finally, the role of endostatin in angiogenesis is less than clear, and only recently has there been some insight gained into whether endostatin has a role in angiogenesis, and if so, how it operates, Benezra & Rafii, Cancer Cell, 205-206, March 2004, see Abstract. For example, Benezra & Rafii teach that endostatin has no role in wound healing or pregnancy, page 206, middle column, second full paragraph. The more

recent review of Benezra & Rafii highlights the current state of the art as to what is known about endostatin as compared to what is taught in earlier documents, such as the '104 patent discussed below that makes reference in the background section thereof that endostatin may be used to control pregnancy, column 6, lines 1-4 of the '104 patent.

Hence, given the heterogeneity of angiogenesis, the uncertain involvement of endostatin in angiogenesis and the uncertain involvement of endostatin in angiogenesis in a particular organ or tissue, the PCT, which focuses on cancer, and non-ocular cancer, provides no teaching of treating neovascularization in the eye.

Regarding claim 33 of the PCT, that claim is directed to a method for making a medicament and not to a method of gene therapy with direct administration to the eye. There is no teaching in claim 33 of directly administering a vector to the eye, instead all claim 33 recites is that the expression product inhibit angiogenesis in the vicinity of the retina.

Clearly, the PCT does not direct the artisan to the claimed method from the extensive list of gene delivery means disclosed therein. Hence, there is no anticipation. Accordingly, withdrawal of the rejection is in order.

II. In item 5 on page 4 of the Office Action, claims 1, 7, 33, 38-41 and 48-50 were rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite.

The rejection is traversed for the following reasons.

While not acquiescing to the position of the Examiner, Applicants have adopted the language proposed by the Examiner to overcome the rejection. Hence, the rejection can be removed.

III. In items 7 and 8 of the Office Action, claims 1, 7, 8, 33, 38-41, 43, 44 and 48-50 were rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. The issue relates to that of the rejection discussed in II above.

The rejection is traversed for the following reasons.

While not acquiescing to the position of the Examiner, Applicants have adopted the language proposed by the Examiner to overcome the rejection. Hence, the rejection can be removed.

IV. In item 10 of the Office Action, claims 1-3, 7, 8, 27-33, 38-41 and 43-50 were rejected under 35 U.S.C. §112, first paragraph, for an alleged want of an enablement.

The rejection is traversed for the following reasons.

The Examiner offered two independent claims that are enabled. Without capitulating to the position of the Examiner and solely to advance prosecution,

Applicants adopted the language offered by the Examiner into a single independent claim.

Hence, withdrawal of the rejection is in order.

V. In item 12 of the Office Action, claims 1-3, 7, 27-29 and 44-47 were rejected under 35 U.S.C. §102(e) over U.S. Pat. No. 6,201,104.

The rejection is traversed for the following reasons.

As discussed in section I above, and herein incorporated by reference, a document that lists a genus with little teaching or guidance as to any one particular element, does not later anticipate claims to that specific element.

The Examiner relies on the background section of the '104 patent, columns 1-6, for teaching a number of hypotheses of angiogenesis and diseases characterized by abnormal angiogenesis and molecules that were thought to have a role in angiogenesis when the '104 patent was filed

However, as discussed in section I above, and herein incorporated by reference, angiogenesis is complex, varies in disease states from normal development, and varies from tissue to tissue. As mentioned hereinabove, a more recent review of the state of the art demonstrates the paucity of information when the '104 patent was filed on the actions, if any, of endostatin on angiogenesis in any one organ or tissue. Thus, the

background of the '104 patent provides no explicit teaching of treating neovascularization of the eye.

Moreover, the section of the detailed description of the '104 patent relied on by the Examiner provides a diffuse summary of gene therapy. Nowhere in the '104 patent is there an explicit teaching of direct administration of an endostatin coding sequence to the eye.

Finally, the '104 patent relates not to endostatin but to polypeptides that bind to endostatin, see the Abstract, detailed description, column 11, last full paragraph, and the claims..

Therefore, as with the PCT discussed above, the '104 patent has no relevance to the instantly claimed subject matter and is a legally insufficient reference for teaching the invention claimed in the instant application. There is no anticipation and the rejection must be removed.

VI. In item 15 of the Office Action, claims 1, 7, 8, 30-32 and 43 were rejected under 35 U.S.C. §103(a) over U.S. Pat. No. 6,201,104 in view of U.S. Pat. No. 6,106,826.

As held by the Examiner, the '104 patent does not teach adenoviral or AAV vectors. To cure that deficiency, the Examiner turned to the '826 patent allegedly to provide such teachings.

The rejection is traversed for the following reasons.

As discussed in section V hereinabove and herein incorporated by reference, the '104 patent is not relevant to the instant application and is legally insufficient to teach gene therapy and particularly the claimed method of administering the particular vectors of interest directly to the eye.

The '826 patent provides a diffuse summary of gene therapy for treating neuronal degeneration. The '826 patent does teach herpes viral vectors, but does not teach any other type of vector.

Column 5 of the '826 patent relied on by the Examiner summarizes means for delivering a gene to a cell but also explicitly teaches that herpes viral vectors are particularly advantageous. The '826 patent at best, mentions adenoviral vectors and AAV vectors as elements in the art. Adenoviral vectors and AAV vectors are not taught in any other fashion in the '826 patent.

In fact, at column 3, lines 49-59, the '826 patent teaches the deficiencies of the use of replication deficient viral vectors, such as adenoviral vectors and AAV vectors. The '826 patent teaches that the better alternative is a herpes virus vector, and more preferably, a replication competent herpes virus vector. The process of developing such vectors encompassed considerable time and experimentation, column 4, line 31 through column 5, line 4. Further advantages of herpes virus vectors can be found in column 5 of the '826 patent.

Thus, the '826 patent teaches away from vectors aside from replication competent herpes virus vectors.

Accordingly, the '826 does not cure the deficiencies of the '104 patent and hence, a prima facie case of obviousness has not been made. In view thereof, withdrawal of the rejection is requested respectfully.

VII. In item 16 of the Office Action, claims 1, 7, 33 and 38 were rejected under 35 U.S.C. §103(a) over U.S. Pat. No. 6,201,104 in view of U.S. Pat. No. 6,555,107.

As held by the Examiner, the '104 patent does not teach lentiviral vectors. To cure that deficiency, the Examiner turned to the '107 patent to provide such teachings.

The rejection is traversed for the following reasons.

As discussed in section V hereinabove and herein incorporated by reference, the '104 patent is not relevant and is legally insufficient to teach gene therapy and particularly the claimed method of administering the particular vectors of interest directly to the eye.

As discussed hereinabove in section I, V and VI as to the other references and herein incorporated by reference, the '107 patent provides a diffuse teaching of gene therapy. A number of methods and means, and a number of target tissues are disclosed without any particularized teaching of direct administration to the eye. Similar

to the references discussed in sections I, V and VI above, the '107 patent does not provide a legally sufficiently teaching of direct administration to the eye.

Thus, the '107 does no more than teach FIV viral vectors, and there is no enabling teaching or suggestion of using such a vector with direct administration to the eye. Accordingly, the '107 patent does not cure the deficiencies of the '104 patent and hence, a prima facie case of obviousness has not been made. In view thereof, withdrawal of the rejection is requested respectfully.

VIII. In item 17 of the Office Action, claims 1, 7, 33 and 38 were rejected under 35 U.S.C. §103(a) over U.S. Pat. No. 6,201,104 in view of U.S. Pat. No. 6,555,107 and U.S. Pat. No. 6,106,826.

The rejection is traversed for the following reasons.

As discussed in section V hereinabove and herein incorporated by reference, the '104 patent is not relevant to the instant application and is legally insufficient to teach gene therapy and particularly the claimed method of administering the particular vectors of interest directly to the eye.

As discussed hereinabove as to the other references in sections I, V and VI and herein incorporated by reference, the '107 patent provides a diffuse teaching of gene therapy. A number of methods and means, and a number of target tissues are disclosed without any particularized teaching to direct administration to the eye. Similar

to the references discussed in sections I, V and VI above, the '107 patent does not provide a legally sufficiently teaching of direct administration to the eye.

Thus, the '107 does no more than teach FIV viral vectors, and there is no enabling teaching or suggestion of using such a vector with direct administration to the eye. Accordingly, the '107 patent does not cure the deficiencies of the '104 patent and hence, a prima facie case of obviousness has not been made.

The '826 patent provides a diffuse summary of gene therapy, as discussed in VI above, and herein incorporated by reference. The '826 does teach making herpes viral vectors, but does not teach making any other type of vector. The '826 patent does not enable gene therapy using any other vector than a herpes viral vector. In fact, the '826 patent teaches away from using any other vectors.

Accordingly, the '826 does not cure the deficiencies of the '104 patent as well as the deficiencies in the combination of the '104 and '107 patents, and hence, a prima facie case of obviousness has not been made.

In view thereof, withdrawal of the rejection is requested respectfully.

CONCLUSION

Applicants submit that the pending claims are in condition for allowance and early indication of such is respectfully requested. Reexamination, reconsideration, withdrawal of the rejections and early passage of the application to issuance are solicited earnestly. If any fees are found to be applicable, please charge any additional fees or make any credits to Deposit Account No. 07-1896.

Respectfully submitted,

Date: September 9, 2004

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